Case Study: Viral-Bacterial Co-Infection Community-Acquired Pneumonia in a Pediatric Patient

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Abstract

Annually, five million cases of viral community-acquired pneumonia occur in pediatric populations in developed countries. A third of cases are dual viral-bacterial co-infections. Some common viral causes of pneumonia in children include respiratory syncytial virus, rhinovirus, influenza, enterovirus, parainfluenza, and coronavirus. Bacterial causes can include *S. pneumoniae*, *H. influenzae*, *M. pneumoniae*, *C. trachomatis*, and *M. catarrhalis*. Symptoms include fever, chills, cough, difficulty breathing, and chest pain. Findings may include retractions, tachypnea, interstitial lung sounds, infiltrates on imaging, and changes in bloodwork. A limited literature review revealed mixed findings for guideline usage in outpatient practice, frequent inappropriate antibiotic prescribing, and non-clinical factors that influenced guideline adherence. A unique case is presented in which the fully immunized school-age child of a homeopathic family presents to an outpatient clinic with classic pneumonia symptoms during the COVID-19 outbreak of 2020. Rapid influenza tests were inconclusive; therefore, a molecular polymerase chain reaction test was performed which returned positive for non-COVID-19 coronavirus, *H. influenza*, *M. catarrhalis*, and *S. pneumonia*. Guidelines endorsed by the American Academy of Pediatrics were utilized and recommendations for natural remedy use were provided. This case encourages judicious use of pediatric pneumonia guidelines throughout a global pandemic in order to determine risk and quarantine recommendations, and to reduce inappropriate antibiotic prescribing.

Keywords: pneumonia, pediatric, coronavirus, antibiotics, case study

Clinical Case Study: Pediatric Community-Acquired Pneumonia

Community-acquired pneumonia (CAP) is a common illness among children in both developed and developing countries. This illness can be viral, bacterial, or combined (Souto, Araújo-Neto, & Nascimento-Carvalho, 2019). Annually, viral CAP has an incidence rate of 100 million cases among children worldwide, of which five million occur in developed countries (Ruuskanen, Lahti, Jennings, & Murdoch, 2011). A third of CAP illnesses in children are dual viral-bacterial co-infections, and 15% of CAP is solely bacterial in etiology (Ruuskanen et al., 2011; Souto et al., 2019). Only a few pediatric cases lead to fatalities in developed countries (Ruuskanen et al., 2011).

The most common viral causes of pneumonia are respiratory syncytial virus, rhinovirus, human metapneumovirus, human bocavirus, influenza, enterovirus, and parainfluenza (Ruuskanen et al., 2011; Souto et al., 2019). Among children age six through 10 years, coronavirus causes of CAP were found second-most frequently yet are not considered a common cause of pneumonia (Spichak et al., 2016). Common bacterial causes of pneumonia are *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, *Chlamydia trachomatis*, and *Moraxella catarrhalis*, in the order of most to least common (Souto et al., 2019). Pediatric vaccines are available to protect against *S. pneumoniae* and *H. influenzae* CAP (Hahn, Heffren, & Abo, 2018).

Clinical CAP symptoms may include sudden-onset fever, chills, cough, difficulty breathing, and pleuritic chest pain (Ruuskanen et al., 2011; Souto et al., 2019). Examination and laboratory findings may include chest retractions, tachypnea, coarse lung sounds, lobar infiltrates or peribronchial thickening on imaging, pneumothorax, and bloodwork that reveals leukocytosis

or neutropenia, elevated C-reactive protein, and variable procalcitonin levels (Ruuskanen et al., 2011; Souto et al., 2019).

Complications of CAP in children can be severe, requiring hospital stays and prolonged antibiotic treatment (Krenke et al., 2018). Complications are local to the respiratory system and include pleural empyema, necrotizing pneumonia, lung abscesses, and severe respiratory syndrome (Krenke et al., 2018; Ruuskanen et al., 2011). Risk factors for and symptoms suggestive of severe complications include the use of ibuprofen or acetaminophen, long duration of fever, and chest pain (Krenke et al., 2018). Protective measures against both CAP and severe complications include childhood receipt of pneumococcal vaccines and a sustained temperature greater than 102.2 degrees Fahrenheit (Dean & Florin, 2018; Krenke et al., 2018). The unwarranted use of anti-pyretic medications in children can worsen CAP severity. Severity of pneumonia is influenced by hypoxemia, age, duration of fever, dehydration, hypotension, the presence of comorbidities, and time to antibiotic therapy (Dean & Florin, 2018).

Limited Literature Review

In a study involving over 1900 pediatric CAP cases among five outpatient pediatric practices, Ambroggio et al. (2018) found that among children over five years of age, hypoxia was infrequently noted, and routine outpatient pulse oximetry use was not supported. This study was performed to evaluate guideline adherence correlation with follow-up visits; notably, chest X-ray (CXR) and complete blood count (CBC) use was low and did not affect the number of antibiotics prescribed (Ambroggio et al., 2018). Over 75% of the children were prescribed an antibiotic according to antibiotic guidelines, yet overall, these were over-prescribed. The antibiotics most frequently prescribed against guideline recommendations were macrolides.

Esposito and Principi (2019) performed an expert narrative review due to the age of pediatric CAP guidelines and concluded that CAP etiology was imprecise in most cases due to the possibility of multiple agents. *S. pneumoniae* was more commonly found in children under age five years, and *M. pneumoniae* was found more frequently in school-age children (Esposito & Principii, 2019). Even without the ability to identify a specific bacterium, ruling out bacterial cause altogether limited unnecessary antibiotic use. Rapid tests for common viruses and influenza reduced ancillary testing and antibiotic use. When these tests are indeterminate, molecular polymerase chain reaction (PCR) testing use is supported and was found to be more sensitive. Imaging can help differentiate between viral and bacterial causes but is unsupported for a majority of mild to moderate outpatient pediatric CAP.

No specific set of symptoms is pathognomonic for pediatric CAP, according to an evidence-based review of guidelines and pediatric CAP cases in emergency settings (Hahn et al., 2018). In children and infants, CAP can manifest subtly or with primarily gastrointestinal symptoms and irritability. Through a literature review, the authors found that hypoxia was contributory to an outpatient CAP diagnosis when the cutoff was set to 96% oxygen saturation. Obtaining bloodwork was not supported for children who were well-appearing and who had prior vaccinations for pneumonia. Antibiotic regimens depended on prior history and community bacterial resistance patterns. High dose amoxicillin was recommended for immunized children. However, 30% of *H. influenzae* is beta-lactamase resistant, requiring a cephalosporin. Macrolide resistance for both *S.* and *M. pneumoniae* bacteria is on the rise; therefore, benefits of macrolide use is unclear.

Macrolide use for treating outpatient CAP was found more frequently in children over five years of age in a retrospective cohort study of over 10,000 children (Handy, Bryan, Gerber,

Zaoutis, & Feemster, 2017). Factors not related to CAP etiology, such as suburban practice and private insurance, were drivers of antibiotic choice, rather than guidelines.

Clinical Case

Demographics and History

In mid-March of 2020, during the COVID-19 pandemic, an eight-year-old Caucasian female presented with respiratory symptoms to an outpatient clinic with a family nurse practitioner specializing in pediatrics. The patient resided in Central Florida with her parents and one sibling. She was of Christian faith, attending church and third grade at a private school. The parent denied any prior cases of influenza, pneumonia, other serious respiratory illnesses or underlying medical issues. The patient's brother had a confirmed case of influenza three months prior. She was fully vaccinated for DTap, Polio, Prevnar, HiB, Hepatitis B, MMR, and Varicella. She had not received an annual influenza vaccine. She was a strict vegan, consuming no animal products or grain. The family home had no pets and the patient had no environmental or medication allergies.

Signs and Symptoms

The mother reported that the patient was experiencing the "worst illness" she had ever witnessed. The symptoms began seven days prior to the visit with a fever as high as 103 degrees Fahrenheit, orally. Her temperature was lowest in the morning hours at 100 degrees which would rise to 102 to 103 degrees every afternoon. The patient reported feeling feverish with chills. She reported a productive cough with clear mucus which worsened with supine positioning, and mild shortness of breath. She reported fatigue and stomach aches with nausea and a decreased appetite, but no vomiting or diarrhea. She had missed school for the past six days. She denied otalgia, ophthalmalgia, nasal congestion, pharyngitis, or body aches. The

mother reported no sick contacts at home and stated that the child had been wearing a mask and performing frequent hand-washing at home to prevent the spread of illness. The child reported that several of her classmates had been ill recently, without specific recall.

The mother had been naturally treating the patient's symptoms daily with the following remedies: Vitamin C, Vitamin D, probiotics, topical essential oils (Breathe by doTERRA, peppermint, lavender, and copaiba), standard process Broncafect and Congaplex, honey syrup, detox bath daily, sublingual Oscillococcinum three times daily, oral Smart Silver, Kids Relief Pain & Fever oral liquid (a homeopathic medicine), oregano, elderberry, saline nasal sprays, and doTERRA DigestZen.

Assessment Findings

The physical exam was positive for a fever of 101.3 degrees Fahrenheit orally, oxygen saturation of 97% on room air, with tachypnea (respiratory rate 26), and tachycardia (heart rate 127). She appeared fatigued with glassy eyes. Her skin was very warm to the touch, dry, and without rash. She had a wet-sounding cough with frequent nose-blowing and rhinorrhea. Nasal turbinates exhibited mild swelling, and the pharynx was mildly erythematous without exudates or swelling. A pea-sized, mobile, tender lymph node was found in the anterior left cervical chain. No retractions or increased work of breathing was noted, and the chest displayed symmetrical movement. Bilateral rhonchi were auscultated which cleared with cough but returned within a few minutes. All other exam findings were within normal limits.

Testing and Interventions

The nurse practitioner administered rapid streptococcus and rapid influenza tests. The influenza test returned a questionable positive result for influenza A with a very faint line, and the streptococcus test was negative. A Diatherix Eurofins molecular testing swab was then

obtained from the pharynx. Within 24 hours, results indicated the patient was positive for coronavirus (non-COVID-19), *H. influenza*, *M. catarrhalis*, and *S. pneumonia*. The test was negative for influenza.

The family was instructed to limit natural treatments to top two choices, with the rationale that their combined over-use can overwhelm a patient's systems. Recommendations were limited to Oscillococcinum TID for the flu-like symptoms, and liposomal Vitamin C for immune-boosting. She was prescribed azithromycin 200mg orally as a loading dose to be followed by 100mg daily on days two through five. The mother was instructed to monitor the patient for increased cough, respiratory distress, or worsening fever, and to report by phone to the provider within 24 hours to give an update.

Outcome

The mother reported that within 24 hours of starting the patient on azithromycin and limiting the natural remedies, the child's fever broke, and her cough started to improve. Return to school was permitted after the fever had broken for 24 full hours and the patient was sufficiently rested; however, due to the COVID-19 outbreak, the child did not return to school for the remainder of the school year.

Discussion

Decision Support Systems

The American Academy of Pediatrics has endorsed the Pediatric Infectious Diseases Society (PIDS) and Infectious Diseases Society of America (IDSA) 2011 guidelines on the management of pediatric CAP (Bradley et al., 2011). Rapid testing should be performed for viral pathogens, and suspicions for *M. pneumoniae* or atypical bacteria warrant a weak recommendation for molecular testing. Blood counts and routine CXRs are unnecessary for

children who are well enough to be treated outpatient (Bradley et al., 2011). In cases where a CXR is recommended, Iorio et al. (2018) found lung ultrasonography (LUS) to be safer and more more effective at imaging lung lesions, compared with radiography. Likewise, Boursiani et al. (2017) found LUS to be of equal efficacy without the risks of radiation exposure. Pulse oximetry is recommended (Bradley et al., 2011).

Antibiotics are not recommended in the absence of findings that suggest bacterial co-infection (Bradley et al., 2011). There are no algorithms available to discern the probable cause of a viral-bacterial co-infection (Ruuskanen et al., 2011). Therefore, if bacterial agents are found via sampling, the individual should be treated with an appropriate antibiotic. Amoxicillin is the first-line therapy of choice for CAP (Bradley et al., 2011; Principi & Esposito, 2018). Macrolides are reserved for school-age children and adolescents when atypical bacteria are found (Bradley et al., 2011). The finding of atypical *M. catarrhalis* in this child over five years of age who was treated outpatient warranted the use of oral azithromycin with a loading dose and a five-day course with weight-based daily dosing (Bradley et al., 2011). Due to the wide spectrum of bacteria etiology, empiric coverage for *S. pneumoniae* was also necessary for this bacterial case; azithromycin for broad spectrum coverage was the appropriate guideline-based choice (Bradley et al., 2011). According to more recent studies, macrolide trials for atypical bacterial CAP were weak or inconclusive (Blythe & Gerber, 2018). Macrolides are effective versus *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*, although resistance is growing (Musher, Sexton, & Bond, 2020).

Adjunct treatment with corticosteroids can be useful for severe obstruction or inflammation (Principi & Esposito, 2018). Findings on Vitamin C and Vitamin D for treatment of childhood CAP were inconclusive (Principi & Esposito, 2018). Hemilä, Louhiala, and Hemilä

(2013) reported mixed findings and insufficient evidence to support the use of Vitamin C. However, supplementation may be reasonable for people with a depleted vitamin C level due to the low cost and low risk.

Homeopathic Oscillococcinum, which is the diluted extract of duck liver and heart, has been used to prevent and treat influenza and other viral illnesses in children (Marrari, Terzan, & Chaufferin, 2012; Ulbricht et al., 2011). Insufficient evidence exists due to poor trial methods; however, there is no evidence of harms for the use of Oscillococcinum (Mathie, Frye, & Fisher, 2015).

Molecular PCR testing has become widely available for the testing of respiratory samples, simplifying diagnostics over previously unreliable nasopharynx aspirates and difficult to capture deep sputum (Ruuskanen et al., 2011). The cost of diagnostic testing to confirm specific pathogens and target treatments can be limiting (Rezkella, Hoover, Hsu, & Lamfers, 2019). The use of PCR to identify pathogens improves outpatient diagnostic testing and antibiotic stewardship (Rezkella et al., 2019). Appropriate PCR utilization decreases unnecessary antibiotic use, slowing rates of drug resistance and extending the usefulness of antibiotics (Rezkella et al., 2019). Nasopharyngeal aspirate is the preferred specimen type among children but requires suction and can be unpleasant for a child (Ruuskanen et al., 2011). In this age group, nasal swabs inserted at a depth of two to three centimeters, and pharyngeal swabs, have similar efficacy and are a viable alternative for PCR sampling (Ruuskanen et al., 2011).

Patient's Perspective

This patient's family preferred as much natural treatment as possible, but also saw the need for prescriptions should they be necessary. The mother preferred that the PCR testing be

performed despite the possibly of non-reimbursement of the high cost. This family strongly desired definite proof of antibiotic need.

Ethical Considerations

Families who prefer to avoid antibiotics may request PCR testing to demonstrate the need for antibiotics. Testing was supported by guidelines due to the length of illness and the child's condition. These tests can be costly and have mixed insurance coverage. Diatherix Eurofins is covered by Medicaid; in the absence of coverage, this test costs $300. In the circumstance of this case, the family planned to request that their private insurance reimburse some of that cost. Mixed insurance mandates can influence testing, the administration of an antibiotic, and the antibiotic selected, thus affecting resistance (Handy et al., 2017). The patient's family was thoroughly educated, and they were encouraged to bring their child in sooner in the absence of improvement for an illness as evident as this CAP case.

Conclusion

This unique case provides insight into viral-bacterial co-infection CAP in an outpatient pediatric patient that was non-COVID-19, occurring mid-pandemic. This case correctly demonstrates the appropriate use of guidelines when atypical bacteria are suspect, and encourages the judicious use of guidelines throughout the COVID-19 pandemic. The high cost of quick-turnaround PCR testing was evident, which may influence patient and provider decision-making, risk to household members, and quarantine recommendations. Furthermore, clinicians who see natural or homeopathic-minded patients in practice should be judicious in their recommendations and education about these remedies for children. Further research is necessary to support the use of macrolides for atypical CAP in children over the use of high-dose amoxicillin. Although azithromycin was effective in this case, guidelines were developed in

2011 and require an update to reflect more recent findings for combined efficacy, safety, reduced antibiotic resistance.

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